



K1532

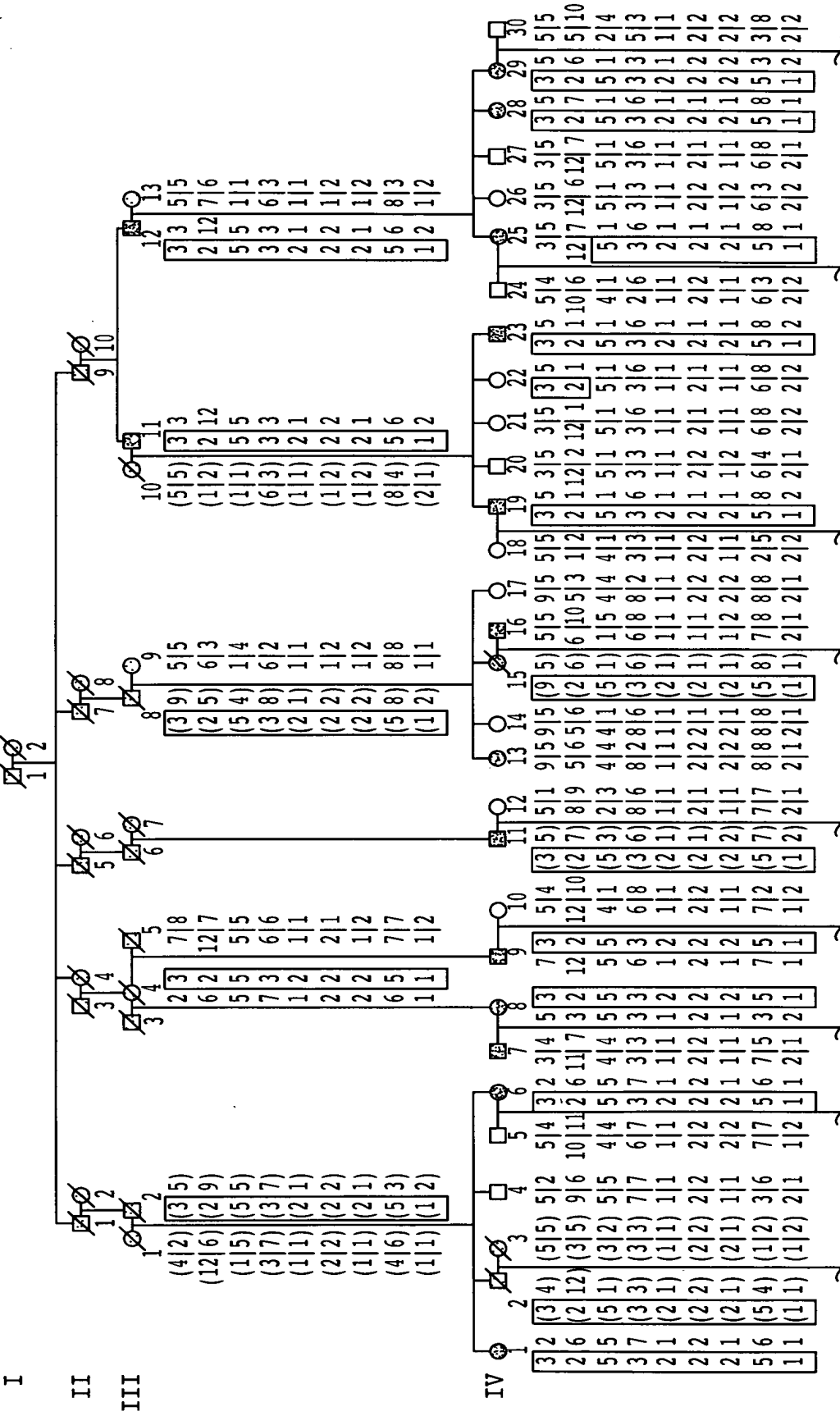
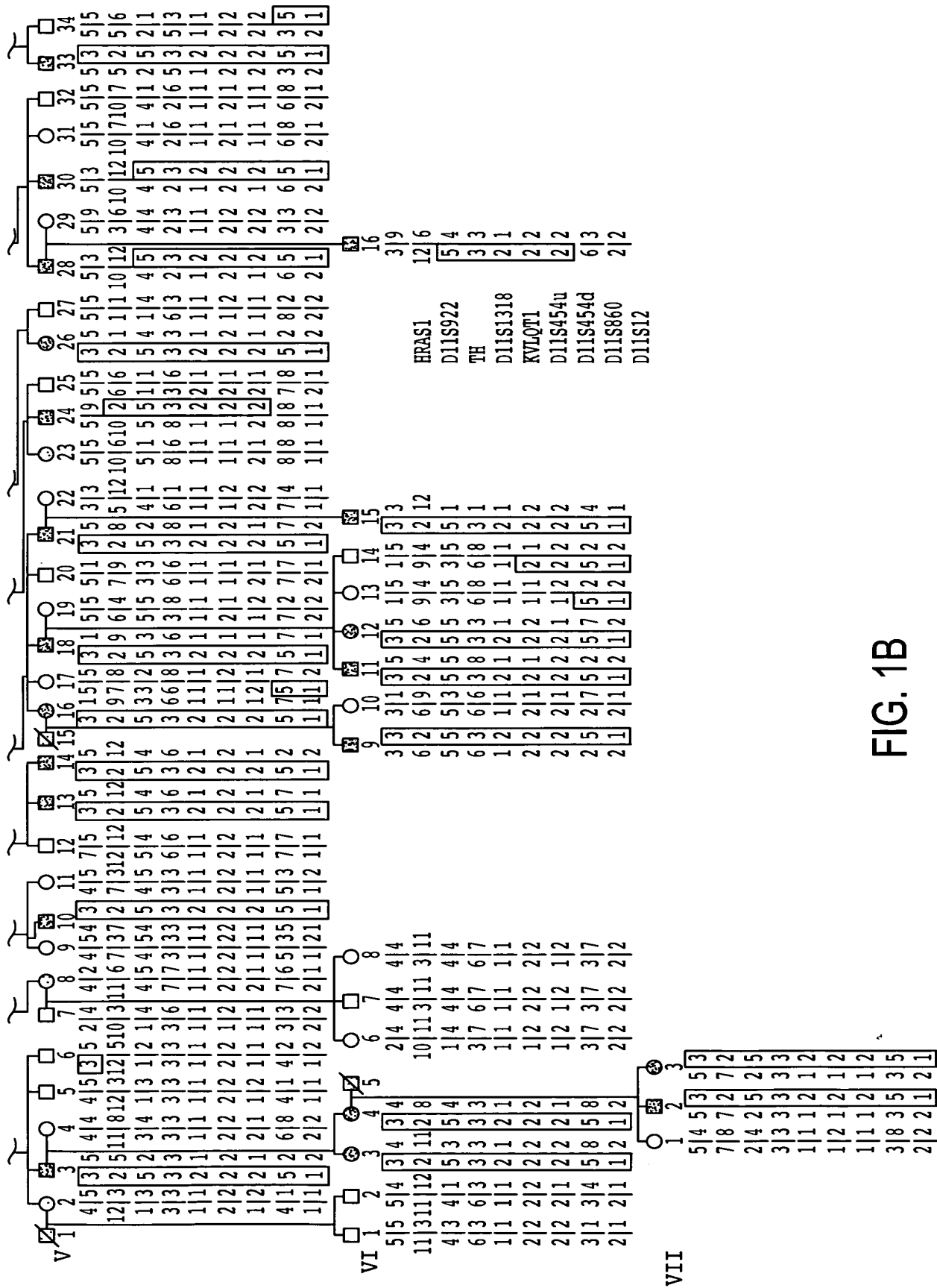


FIG. 1A



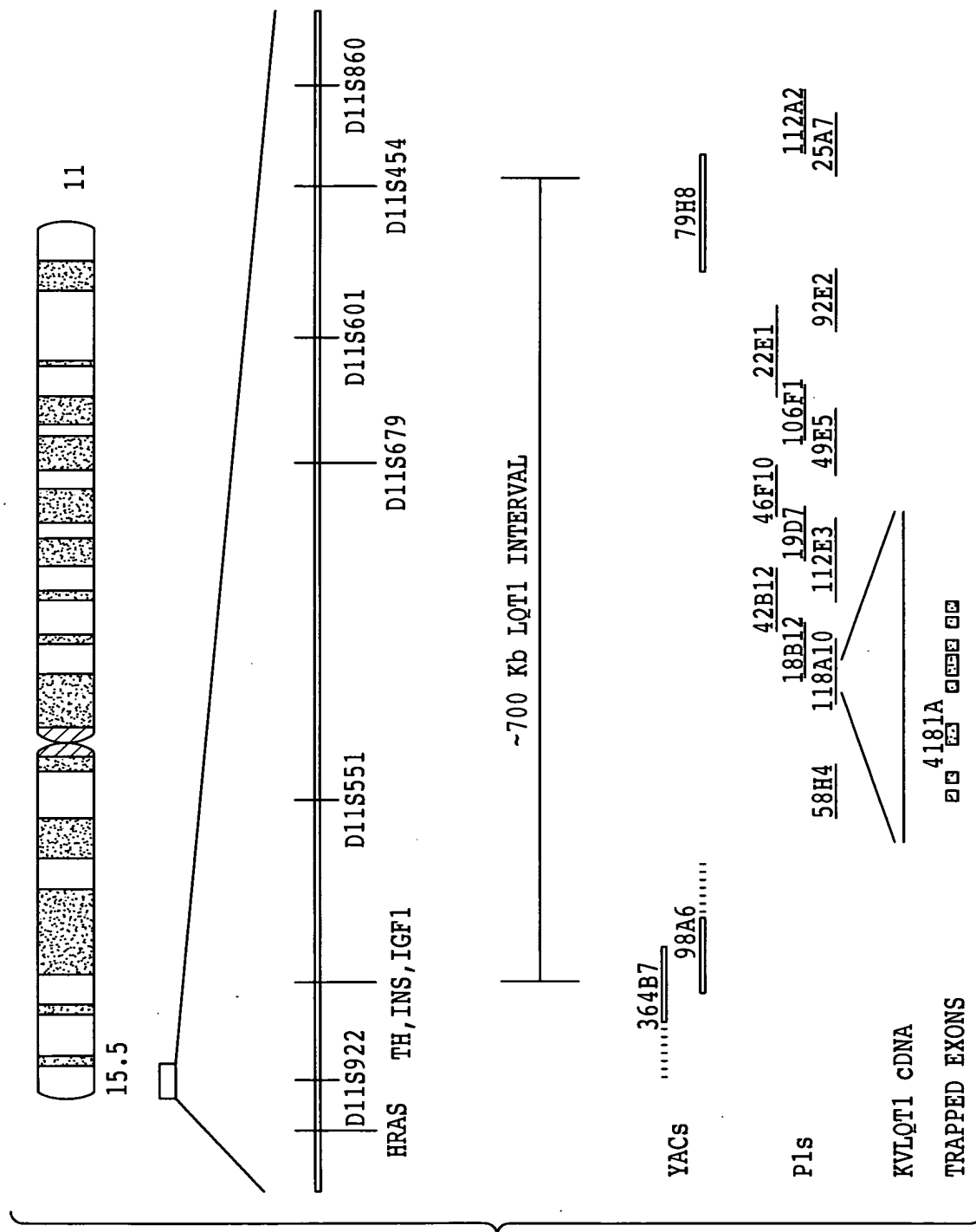


FIG. 2

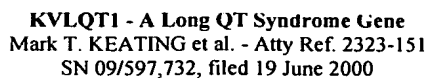


FIG. 3



KVLQT1 - A Long QT Syndrome Gene
Mark T. KEATING et al. - Atty Ref. 2323-151
SN 09/597,732, filed 19 June 2000

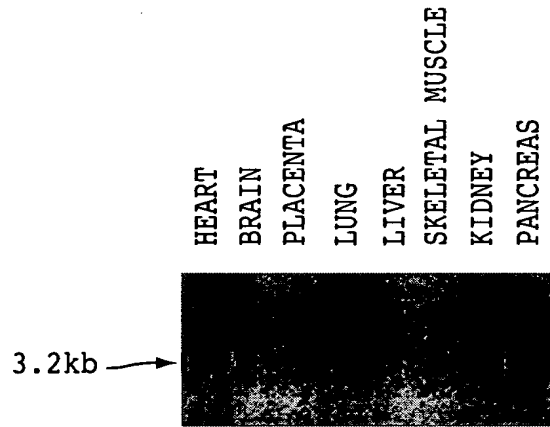


FIG. 4



CTGCCCCCTCCGGCCCCGCCCCGAGCGCCCGGGCTGGGCGCGGAGCGGCCCCCGCGGGGGCTGGCAGCAGTGGCTGCC-81
CGCACTGCGCCCGGGCGCTCGCTTCGCTGCAGCTCCCGGTGCGCGCGCTCGGGCGGCCCCCGGCAGGCCCTCCTCGTT-162
ATGGCCGCGGCCCTCCTCCCCGCGAGGGCCGAGAGGAAGCGCTGGGGTGGGGCGCCCTGCCAGCGCCCCGGCGGGGCAGC-243
M A A A S S P P R A E R K R W G W G R L P G A R R G S -27
GCGGGCTGGCAAGAAGTCCCCCTTCTCGCTGGAGCTGGCGGAGGGCGGGCGGGCGGGCGGCTCTACGCGCCATC-324
A G L A K K C P F S L E L A E G G P A G G A L Y A P I -54
GCGCCCGGCGCCCGAGGTCCCGCGCCCCCTGCGTCCCGGCGCGCCCGCGCGCCCCAGTTGCTTCCGACCTTGGCCCG-405
A P G A P G P A P P A S P A A P A A P P V A S D L G P -81
CGGCCGCGGTGAGCCTAGACCGCGCGTCTCCATCTACAGCACGCGCGCCCGGTGTTGGCGCGCACCCACGTCCAGGGC-486
R P P V S L D P R V S I Y S T R R P V L A R T H V Q G -108
CGCGTCTACAACCTCCTCGAGCGTCCACCGGCTGGAATGCTTCGTTTACCACCTTCGCGCTCTCCTCATCGTCTGGTC-567
R V Y N F L E R P T G W K C F V Y H F A V F L I V L V -135
TGCCTCATCTTCAGCGTGCTGTCCACCATCGAGCAGTATGCCGCCCTGGCCACGGGGACTCTCTTCTGGATGGAGATCGTG-648
C L I F S V L S T I E Q Y A A L A T G T L F W M E I V -162
CTGGTGGTGTCTTCTCGGGACGGAGTACGTGGTCCGCCTCTGGTCCCGCGGCTGCCGCGAGCAAGTACGTGGGCTCTGGGGG-729
L V V F F G T E Y V V R L W S A G C R S K Y V G L W G -189
CGGCTGCGCTTTGCCCCGAAGCCCATTTCCATCATCGACCTCATCGTGGTCTGGCTCCATGGTGGTCTCTGCGTGGGC-810
R L R F A R K P I S I I D L I V V V A S M V V L C V G -216
TCCAAGGGGAGGTGTTTGGCCAGTCCGGCCATCAGGGGCATCCGCTTCTGCGATCCTGAGGATGCTACACGTCGACCGC-891
S K G Q V F A T S A I R G I R F L Q I L R M L H V D R -243
CAGGGAGGCACCTGGAGGCTCCTGGGCTCCGTGGTCTTCATCCACCGCCAGGAGCTGATAACCACCTGTACATCGGCTTC-972
Q G G T W R L L G S V V F I H R Q E L I T T L Y I G F -270
CTGGGCTCATCTTCTCCTCGTACTTTGTGTACTGGCTGAGAAGGACGCGGTGAACGAGTCAGGCCGCGTGGAGTTCGGC-1053
L G L I F S S Y F V Y L A E K D A V N E S G R V E F G -297
AGCTACGCAGATGCGCTGTGGTGGGGGGTGGTACAGTCACCCACCATCGGCTATGGGGACAAGGTGCCCCAGACGTGGGTC-1134
S Y A D A L W W G V V T V T T I G Y G D K V P Q T W V -324
GGGAAGACCATCGCCTCCTGCTTCTGTCTTTGCCATCTCCTTCTTTGCGCTCCAGCGGGGATTCTTGGCTCGGGGTTT-1215
G K T I A S C F S V F A I S F F A L P A G I L G S G F -351
GCCCTGAAGGTGCAGCAGAAGCAGAGGCAGAAGCACTTCAACCGGCAGATCCCGCGGCAGCCTCACTCATTAGACCGCA-1296
A L K V Q Q K Q R Q K H F N R Q I P A A A S L I Q T A -378
TGGAGGTGCTATGCTGCCGAGAACCCCGACTCCTCCACCTGGAAGATCTACATCCGGAAGGCCCCCGGAGCCACACTCTG-1377
W R C Y A A E N P D S S T W K I Y I R K A P R S H T L -405
CTGTCACCCAGCCCCAAACCAAGAAGTCTGTGGTGGTAAAGAAAAAAGTTCAAGCTGGACAAAGACAATGGGGTGA-1458
L S P S P K P K K S V V V K K K K F K L D K D N G V T -432
CCTGGAGAGAAGATGCTCACAGTCCCCATATCACGTGCGACCCCCAGAAGAGCGGCGGCTGGACCACTTCTCTGTGAC-1539
P G E K M L T V P H I T C D P P E E R R L D H F S V D -459
GGCTATGACAGTTCTGTAAGGAAGAGCCCAACACTGCTGGAAGTGAGCATGCCCCATTTTCATGAGAACCAACAGCTTCGCC-1620
G Y D S S V R K S P T L L E V S M P H F M R T N S F A -486
GAGGACCTGGACCTGGAAGGGGAGACTCTGTGACACCCATCACCCACATCTCACAGCTGCGGGAACACCATCGGGCCACC-1701
E D L D L E G E T L L T P I T H I S Q L R E H H R A T -513
ATTAAGGTCATTTCGACGCATGCAGTACTTTGTGGCCAAGAAGAAATTCAGCAAGCGCGGAAGCCTTACGATGTGCGGGAC-1782
I K V I R R M Q Y F V A K K K F Q Q A R K P Y D V R D -540
GTCATTGAGCAGTACTCGCAGGGCCACCTCAACCTCATGGTGGCATCAAGGAGCTGCAGAGGAGGCTGGACCACTCCATT-1863
V I E Q Y S Q G H L N L M V R I K E L Q R R L D Q S I -567

FIG. 5A



GGGAAGCCCTCACTGTTTCATCTCCGTCTCAGAAAAGAGCAAGGATCGCGGCAGCAACACGATCGGCGCCCGCCTGAACCGA-1944
G K P S L F I S V S E K S K D R G S N T I G A R L N R -594

GTAGAAGACAAGGTGACGCAGCTGGACCAGAGGCTGGCACTCATCACCACATGCTTCACCAGCTGCTCTCCTTGACGGT-2025
V E D K V T Q L D Q R L A L I T D M L H Q L L S L H G -621
GGCAGCACCCCGGCAGCGGGCGGCCCCCAGAGAGGGGCGGGCCACATCACCAGCCCTGCGGCAGTGGCGGCTCCGTC-2106
G S T P G S G G P P R E G G A H I T Q P C G S G G S V -648
GACCCTGAGCTCTTCTGCCCAGCAACACCTGCCCACCTACGAGCAGCTGACCGTGCCAGGAGGGGCCCCGATGAGGGG-2187
D P E L F L P S N T L P T Y E Q L T V P R R G P D E G -675
TCCTGAGGAGGGGATGGGGCTGGGGGATGGGCCCTGAGTGAGAGGGGAGGCCAAGAGTGGCCCCACCTGGCCCTCTCTGAAG-2268
S * -676
GAGGCCACCTCCTAAAAGGCCAGAGAGAAGAGCCCCACTCTCAGAGGCCCCAATACCCCATGGACCATGCTGTCTGGCAC-2349
AGCCTGCACTTGGGGGCTCAGCAAGGCCACCTCTTCTGGCCGGTGTGGGGGCCCCGTCTCAGGTCTGAGTTGTTACCCCA-2430
AGCGCCCTGGCCCCCAGTGGTGTGTTGACATCACTGGCATGGTGGTGGGACCCAGTGGCAGGGCACAGGGCCTGGCCCC-2511
ATGTATGGCCAGGAAGTAGCACAGGCTGAGTGACAGGCCCCACCTGCTTGGCCCAGGGGGCTTCTGAGGGGAGACAGAGCA-2592
ACCCCTGGACCCAGCCTCAAATCCAGGACCTGCCAGGCACAGGCAGGGCAGGACCAGCCACGCTGACTACAGGGCCAC-2673
CGGCAATAAAAGCCCAGGAGCCCATTTGGAGGGCCTGGGCCTGGCTCCCTCACTCTCAGGAAATGCTGACCCATGGGCAGG-2754
AGACTGTGGAGACTGCTCCTGAGCCCCAGCTTCCAGCAGGAGGGACAGTCTCACCATTCCCCAGGGCACGTGGTTGAGT-2835
GGGGGAACGCCCCTTCCCTGGGTTAGACTGCCAGCTCTTCTAGCTGGAGAGGAGCCCTGCCTCTCCGCCCCCTGAGCCC-2916
ACTGTGCGTGGGGCTCCCGCCTCCAACCCCTCGCCAGTCCCAGCAGCCAGCCAAACACAGAGGGGACTGCCACCTCC-2997
CCTTGCCAGCTGCTGAGCCGAGAGAAGTGACGGTTCCTACACAGGACAGGGGTTCCTTCTGGGCATTACATCGCATAGAA-3078
ATCAATAATTTGTGGTGATTTGGATCTGTGTTTAAATGAGTTTCACAGTGTGATTTTGATTATTAATTGTGCAAGCTTTTC-3159
CTAATAAACGTGGAGAATCAC(A)_n -3180

FIG. 5B



KVLQT1 - A Long QT Syndrome Gene
Mark T. KEATING et al. - Atty Ref. 2323-151
SN 09/597,732, filed 19 June 2000

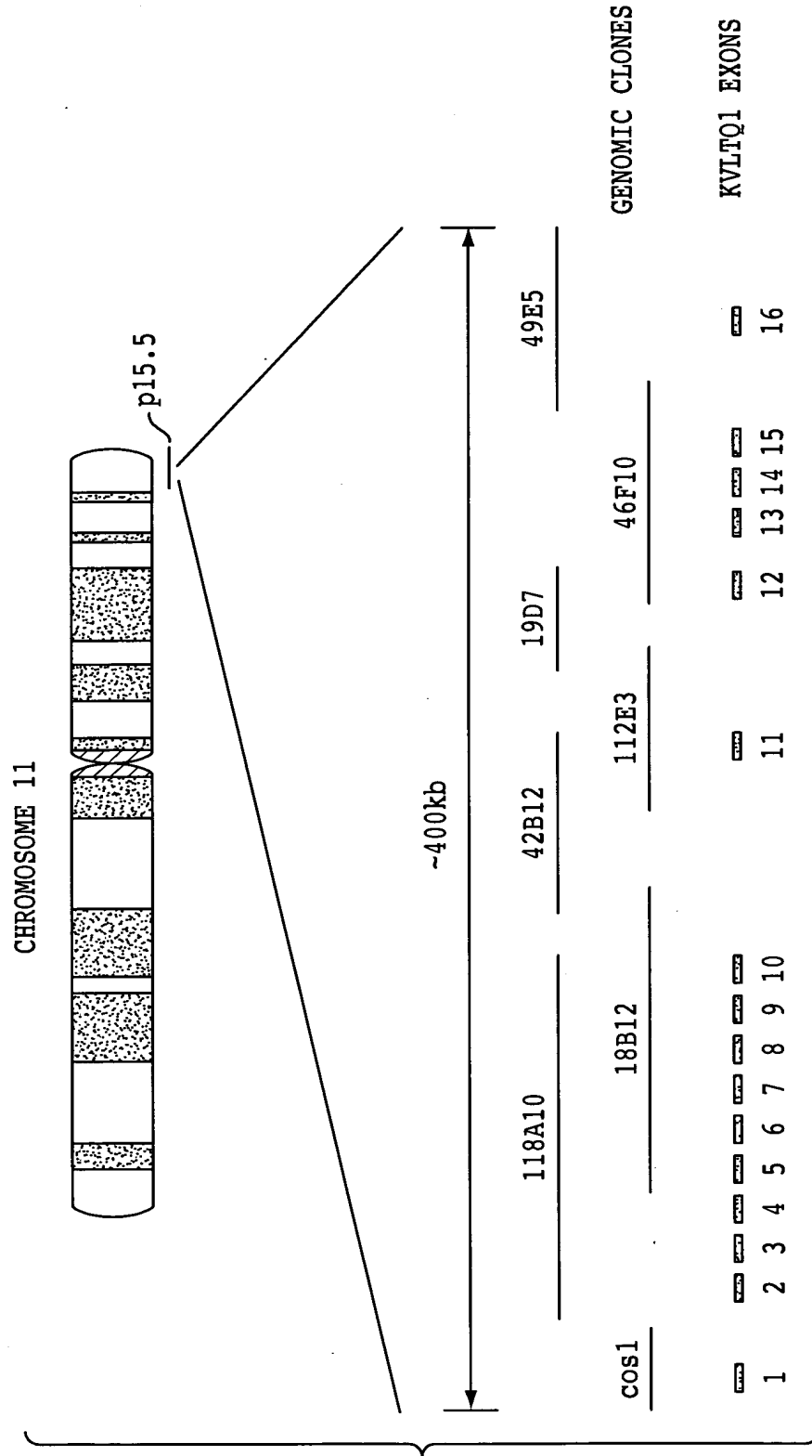


FIG. 6

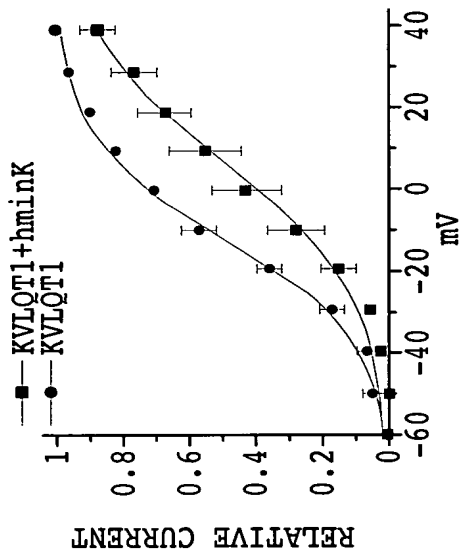


FIG. 7B

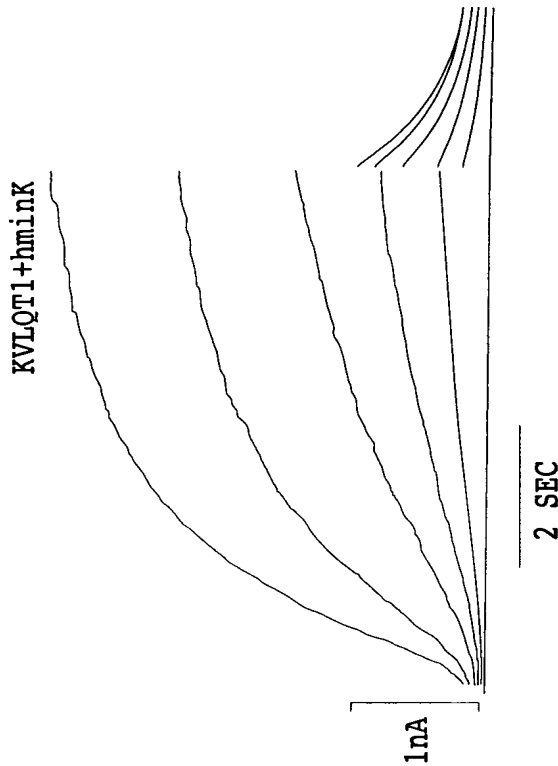


FIG. 7E

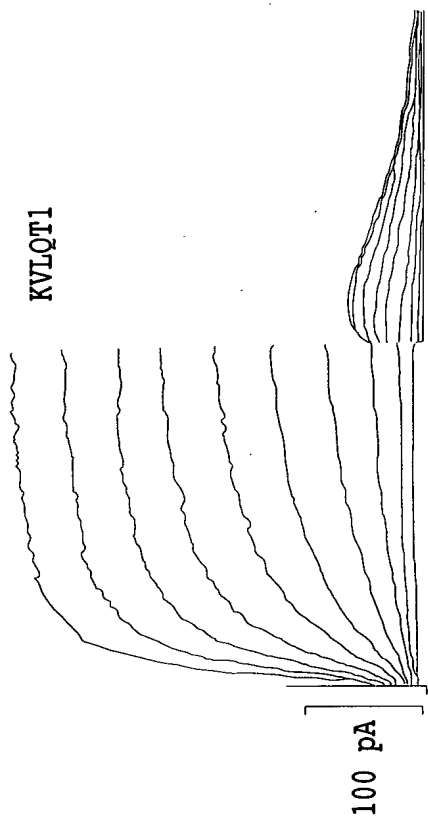


FIG. 7A

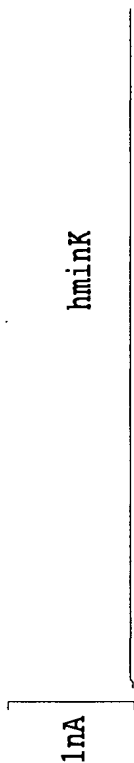


FIG. 7C

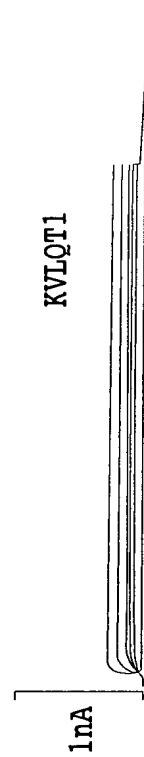
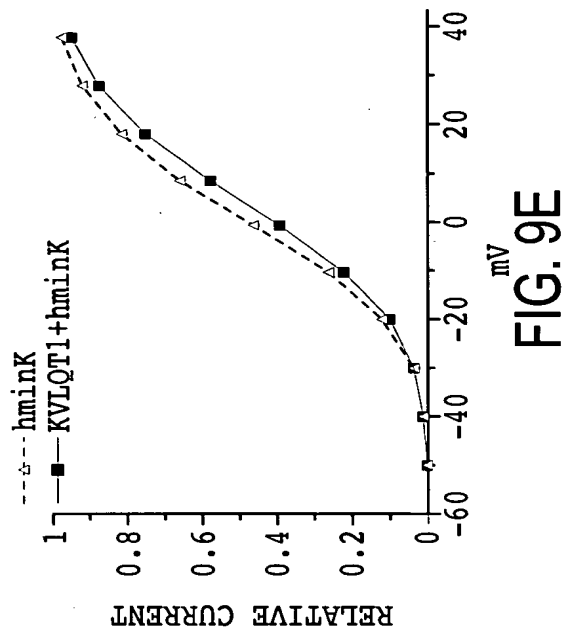
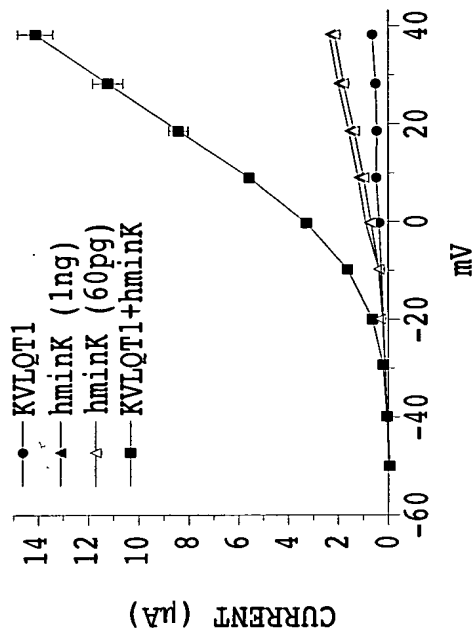
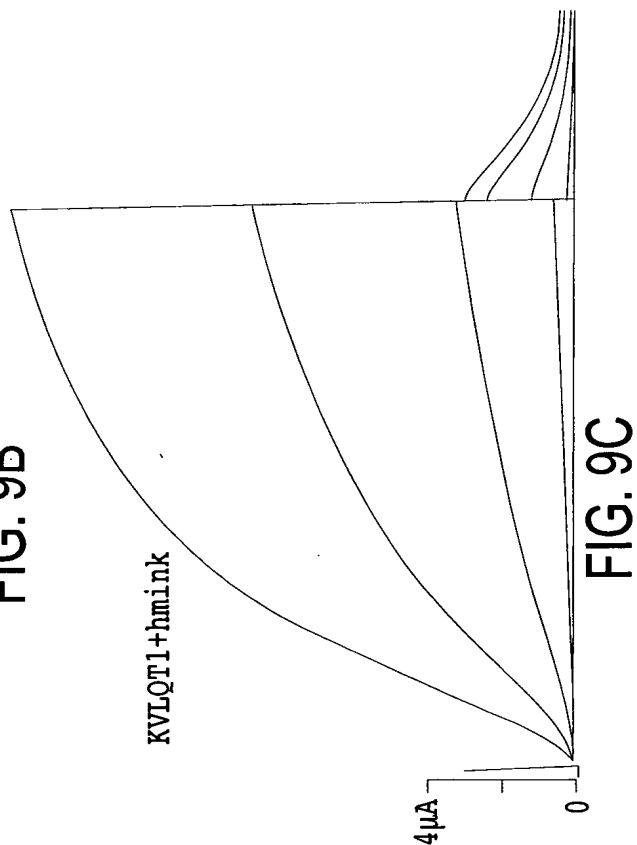
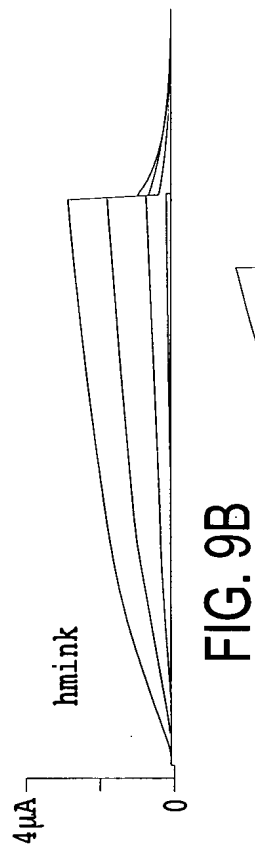
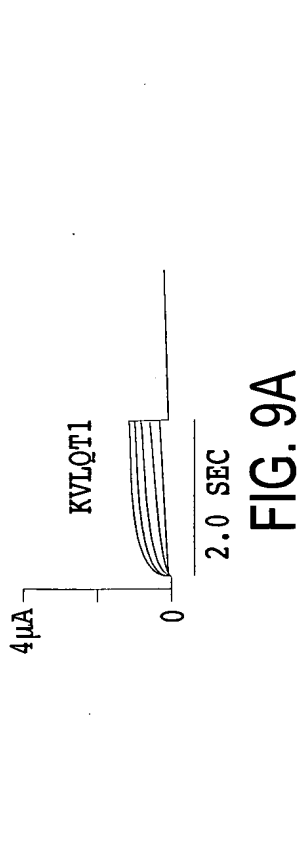


FIG. 7D



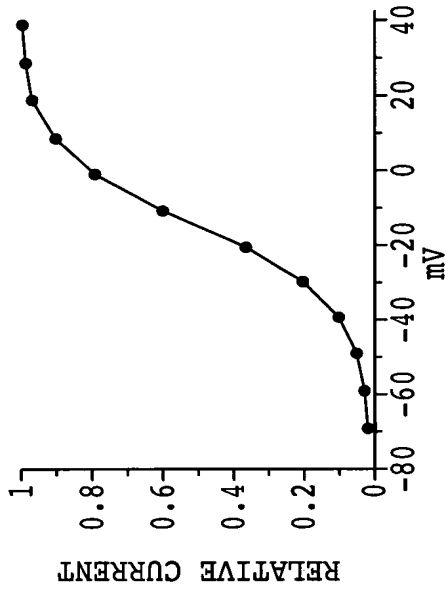


FIG. 8B

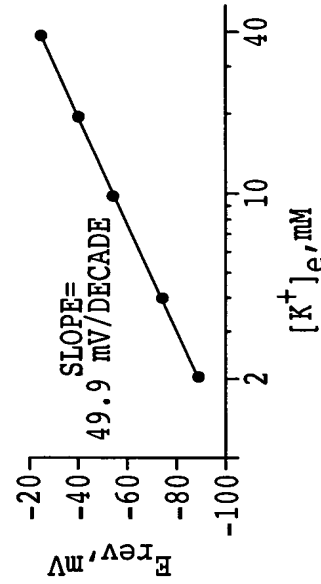


FIG. 8C

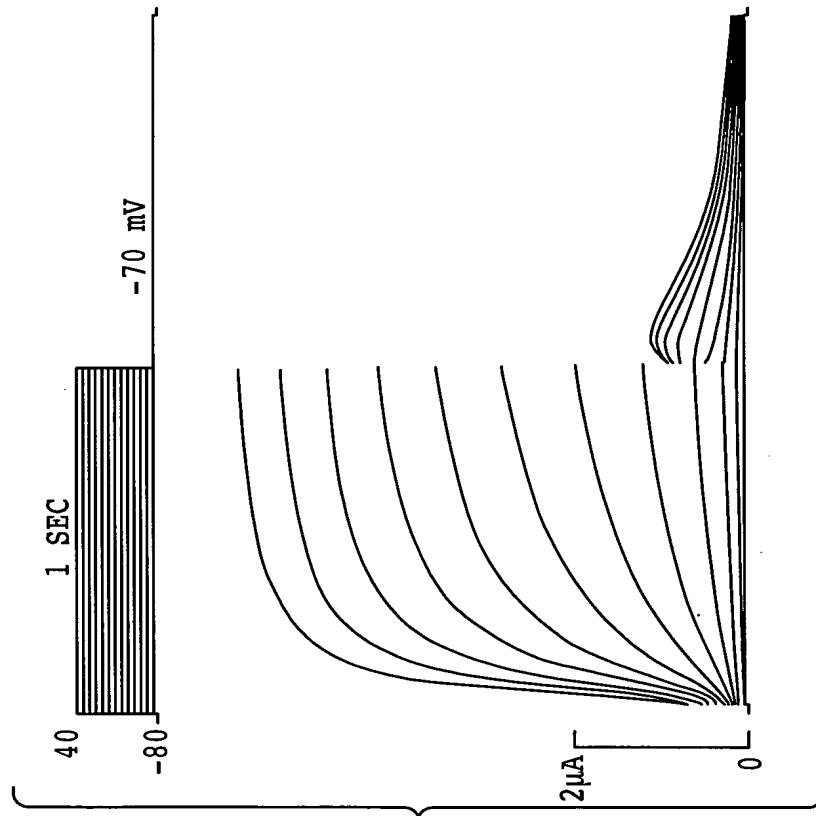


FIG. 8A



KVLQT1 - A Long QT Syndrome Gene
Mark T. KEATING et al. - Atty. Ref. 2323-151
SN 09/597,732, filed 19 June 2000

XENOPUS MNENAINSLYEAIPLPDGSSNGRQEDRQANSFELKRETLVATDPPRPT

HUMAN QGRVYNFLERPTGWKCFVYHFAVFLIVL
|||||

XENOPUS INLDPRVSIYSGRRPLFSRTNIQGRVYNFLERPTGWKCFVYHFTVFLIVL

HUMAN S1_____S2_____
VCLIFSVLSTIEQYAALATGTLFWMEIVLVVFFGTEYVVRLWSAGCRSKY
|||||

XENOPUS ICLIFSVLSTIQYNNLATETLFWMEIVLVVFFGAEYVVRLWSAGCRSKY

HUMAN VGLWGRLRFARKPISIIDLIVVVASMVVLCVGSKGQVFATSAIRGIRFLQ
| |||||

XENOPUS VGVWGRLRFARKPISVIDLIVVVASVIVLCVGSNGQVFATSAIRGIRFLQ
A

HUMAN ILRMLHVDROGGTWRLGSSVFIHRQELITTLYIGFLGLIFSSYFVYLAE
|||||

XENOPUS ILRMLHVDROGGTWRLGSSVFIHRQELITTLYIGFLGLIFSSYFVYLAE

HUMAN KDAVNESGRVEFGSYADALWWGVVTVTTIGYGDKVPQTWVGKTIASCFSV
||| || |||||

XENOPUS KDAIDSSGEYQFGSYADALWWGVVTVTTIGYGDKVPQTWIGKTIASCFSV

HUMAN S6_____
FAISFFALPAGILGSGFALKVQOKQKQKHFNRIIPAAASLIQTAWRCYAA
|||||

XENOPUS FAISFFALPAGILGSGFALKVQOKQKQKHFNRIIPAAASLIQTAWRCYAA

HUMAN ENPDSSTWKIYIRKAPRSHTLLSPSPKPKKSVVVKKKKFKLDKDNVTPG
|||||

XENOPUS ENPDSATWKIYIRKQSRNHHIMSPSP

HUMAN EKMLTVPHITCDPPEERRLDHFSVDGYDSSVRKSPTLLEVSMPHFMRTNS

HUMAN FAEDLDLEGETLLTPITHISQLREHHRATIKVIRRMQYFVAKKKFQOARK

HUMAN PYDVRDVIEQYSQGHNLNMRVIKELQRRLDQSIGKPSLFISVSEKSKDRG

HUMAN SNTIGARLNRVEDKVTQLDQRLALITDMLHQLLSLHGGSTPGSGGPPREG

HUMAN GAHITQPCGSGGSVDPELFLPSNTLPTYEQLTVPRRGPDDEGS

FIG. 10

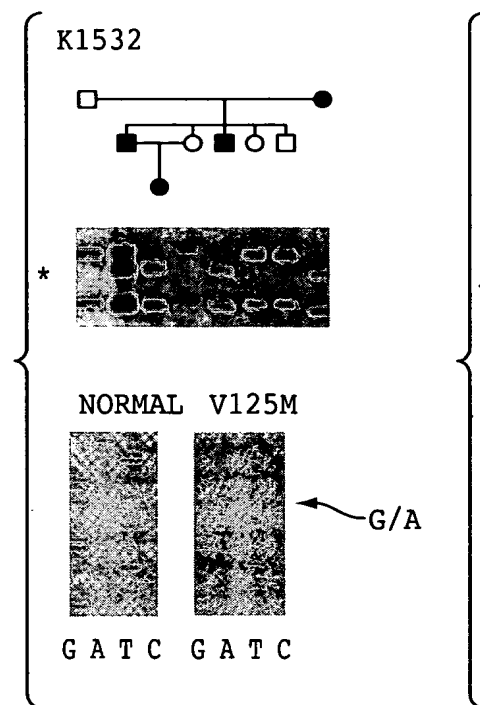


FIG. 11A

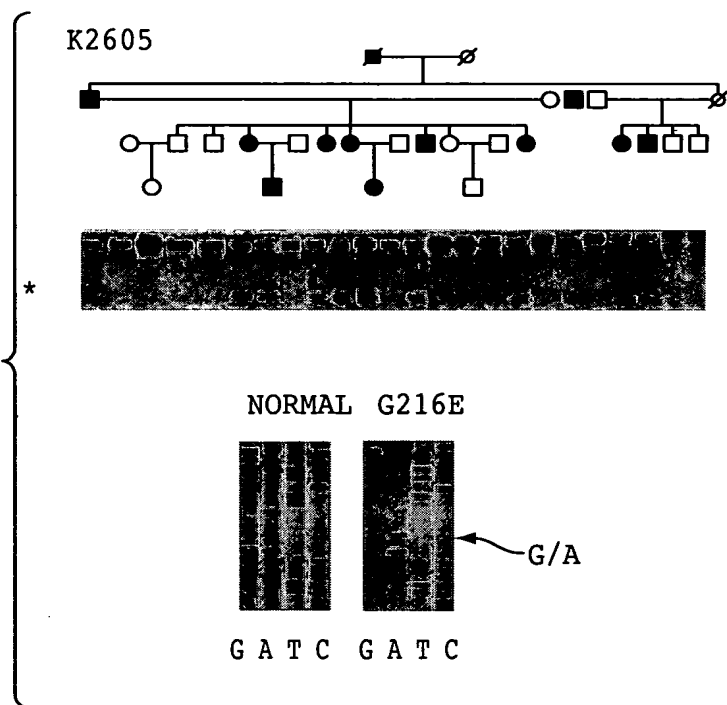


FIG. 11B

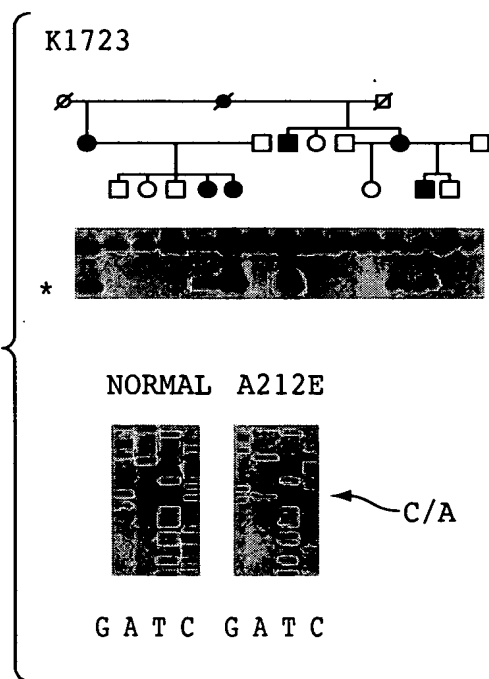


FIG. 11C

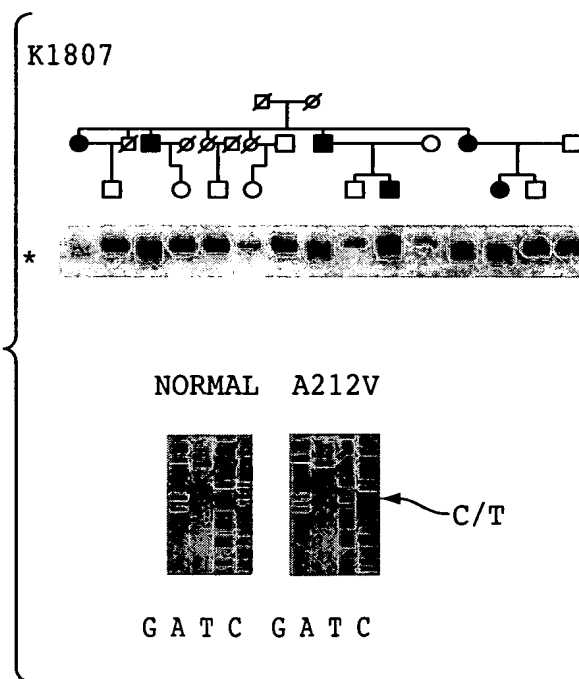
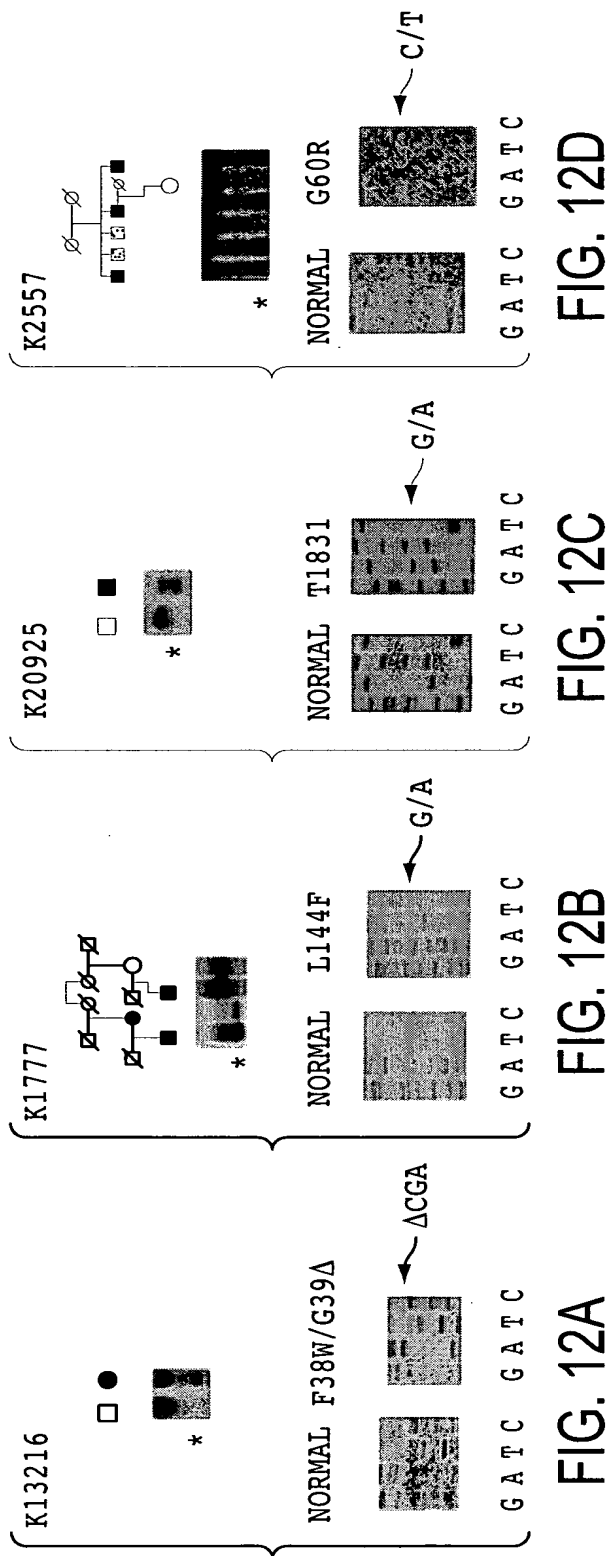


FIG. 11D



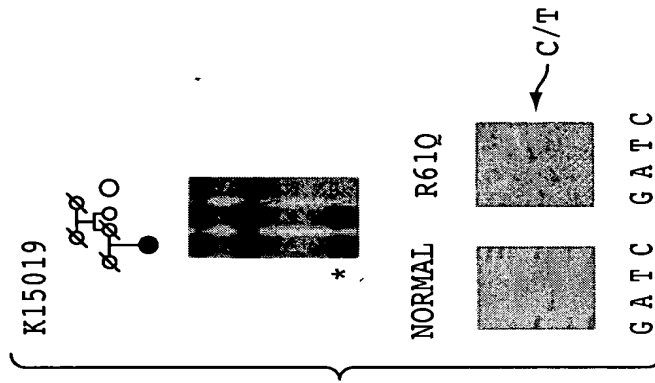


FIG. 12G

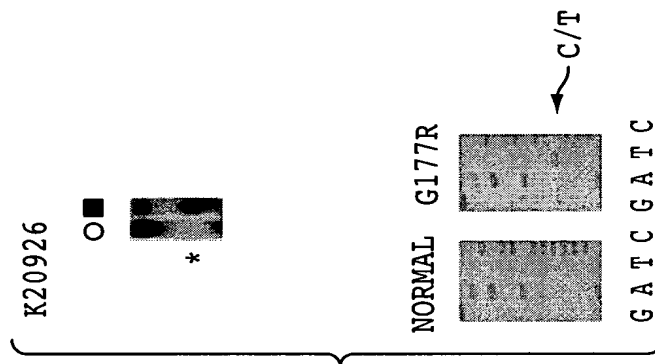


FIG. 12F

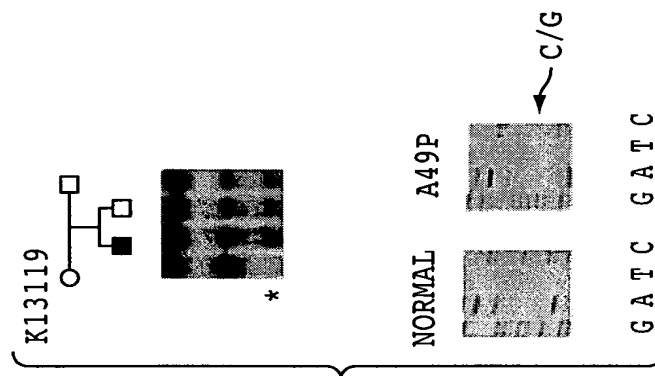


FIG. 12E

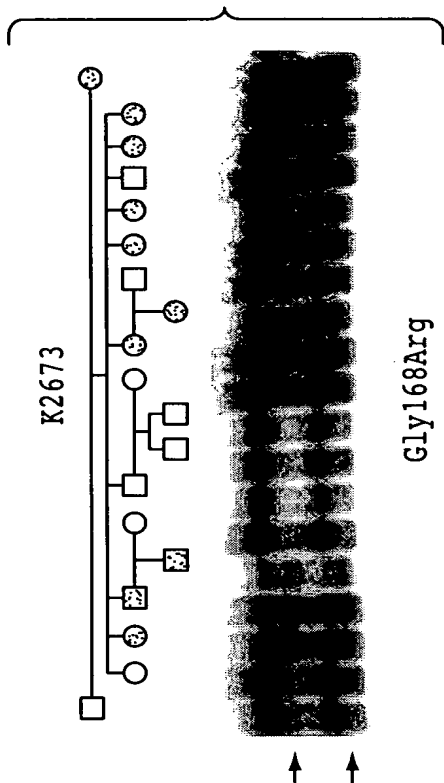


FIG. 12I

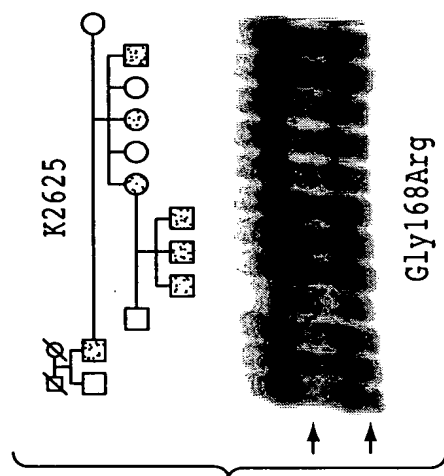


FIG. 12H

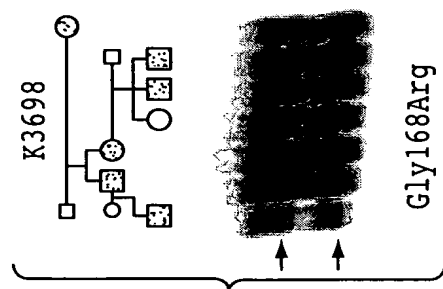


FIG. 12J

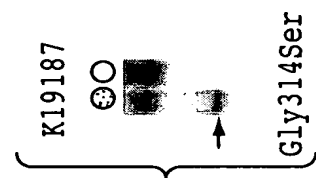


FIG. 12K



FIG. 12L

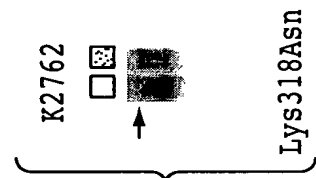


FIG. 12M

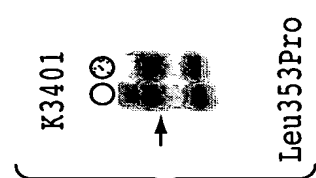


FIG. 12N

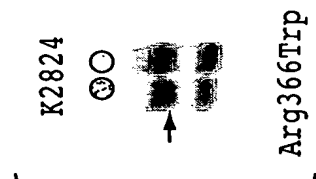
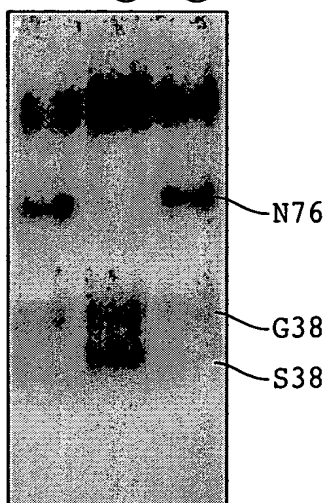
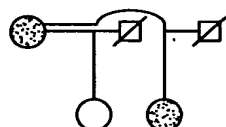


FIG. 12O



K1789

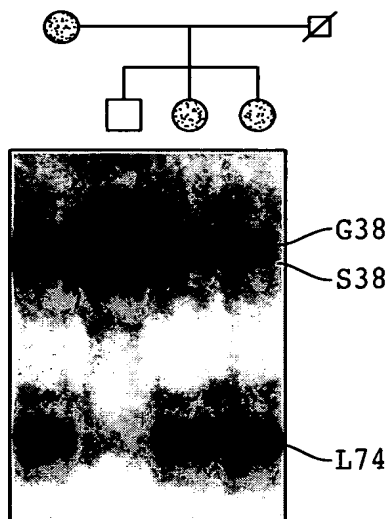


NORMAL	CAC H	TCG S	AAC N	GAC D	CCA P	TTC F	AAC N
MUTANT	CAC H	TCG S	AAC N	AAC N	CCA P	TTC F	AAC N

FIG. 13A



K1754



NORMAL	CTG	GAG	CAC	TCG	AAC	GAC	CCA
	L	E	H	S	N	D	P
				↓			
MUTANT	CTG	GAG	CAC	TTG	AAC	GAC	CCA
	L	E	H	L	N	D	P

FIG. 13B



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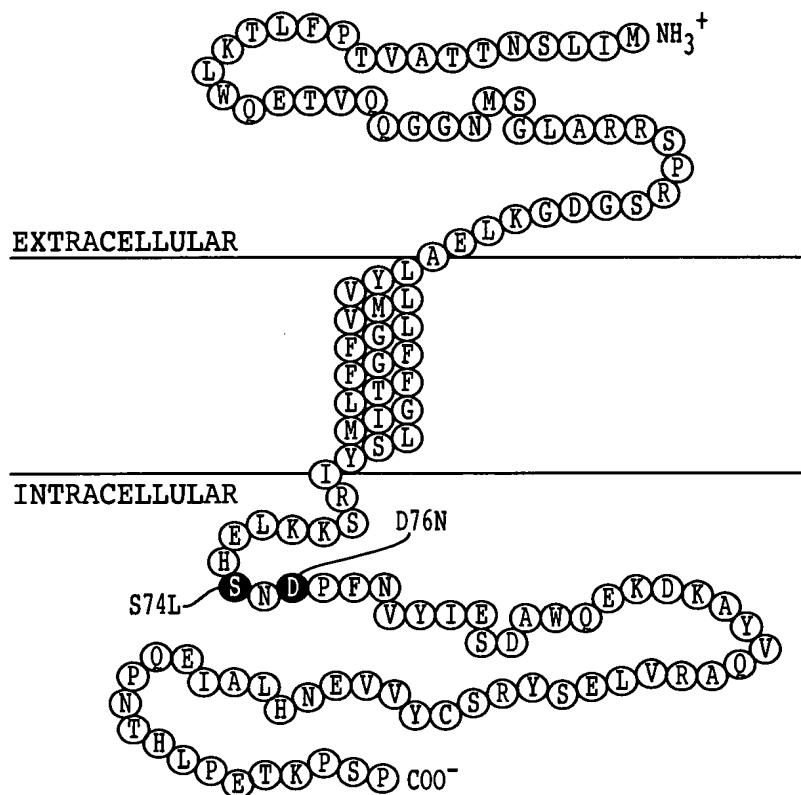


FIG. 13C

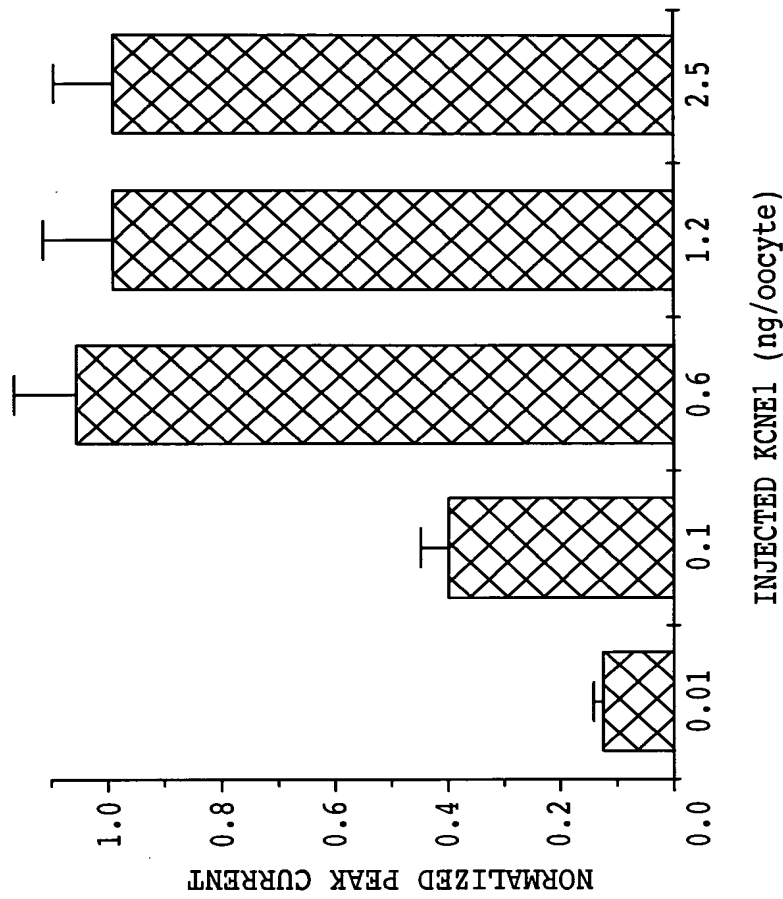


FIG. 14B

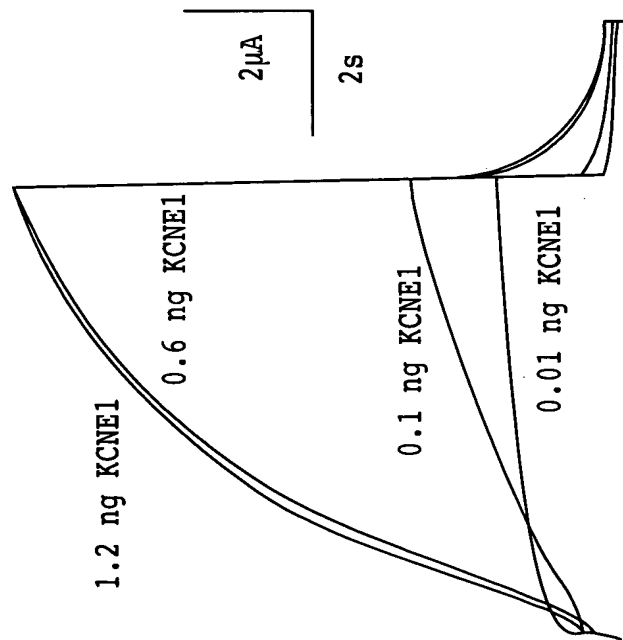


FIG. 14A

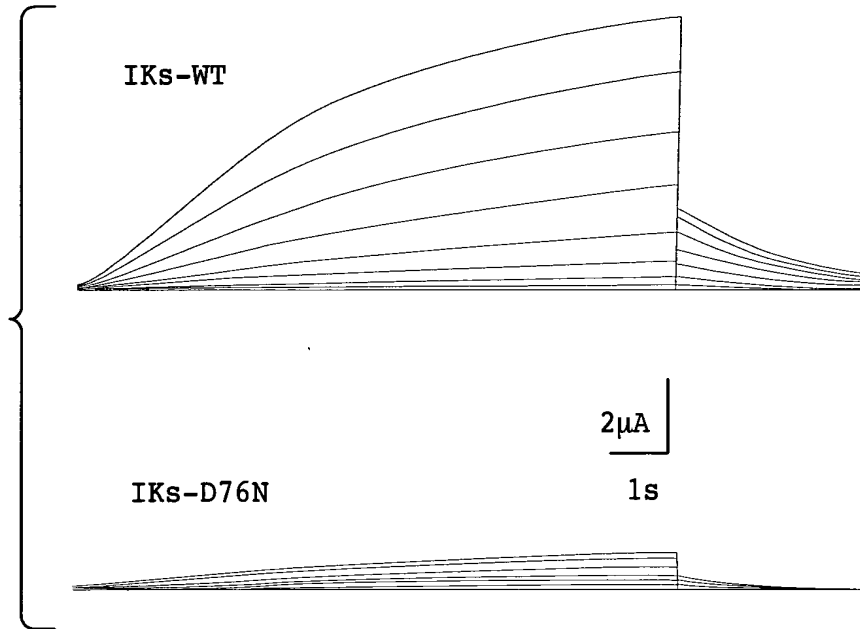


FIG. 15A

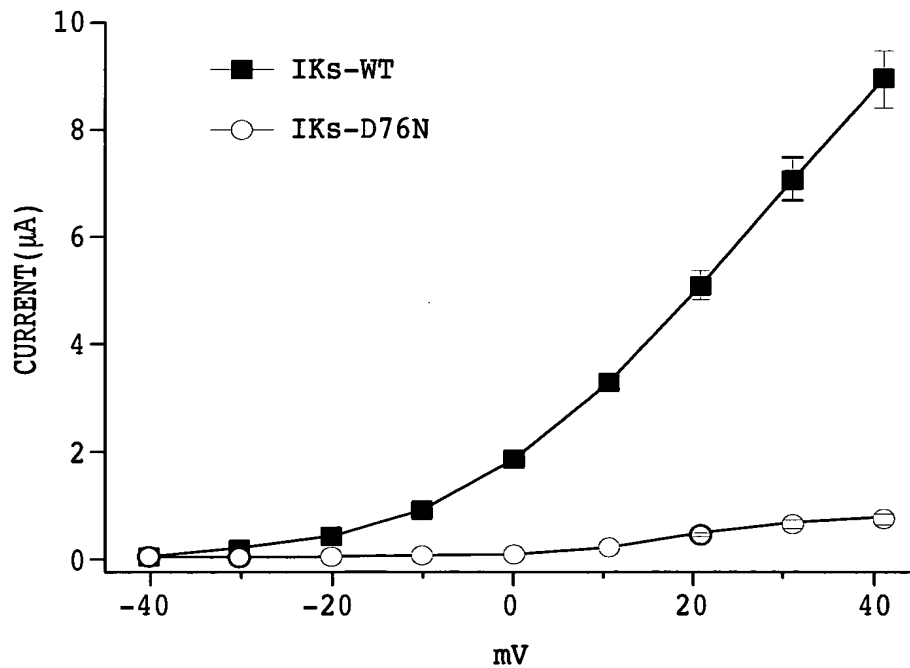


FIG. 15B

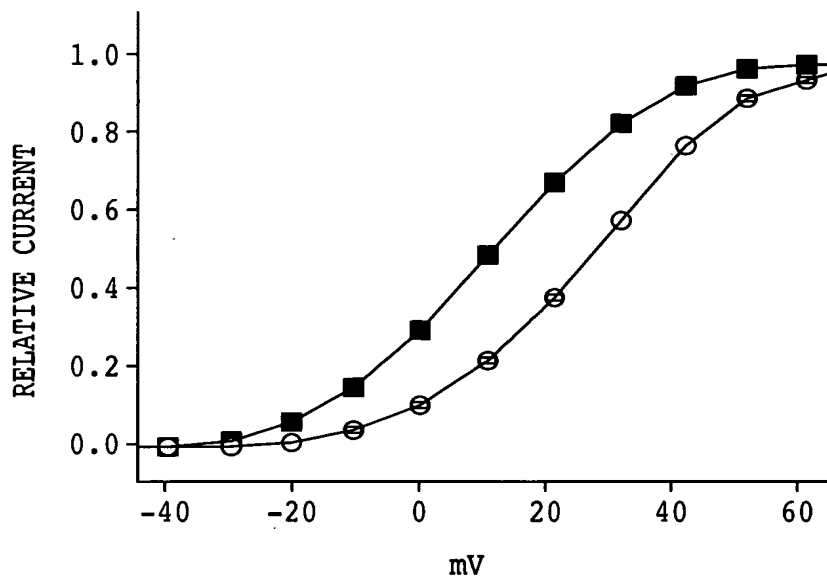


FIG. 15C

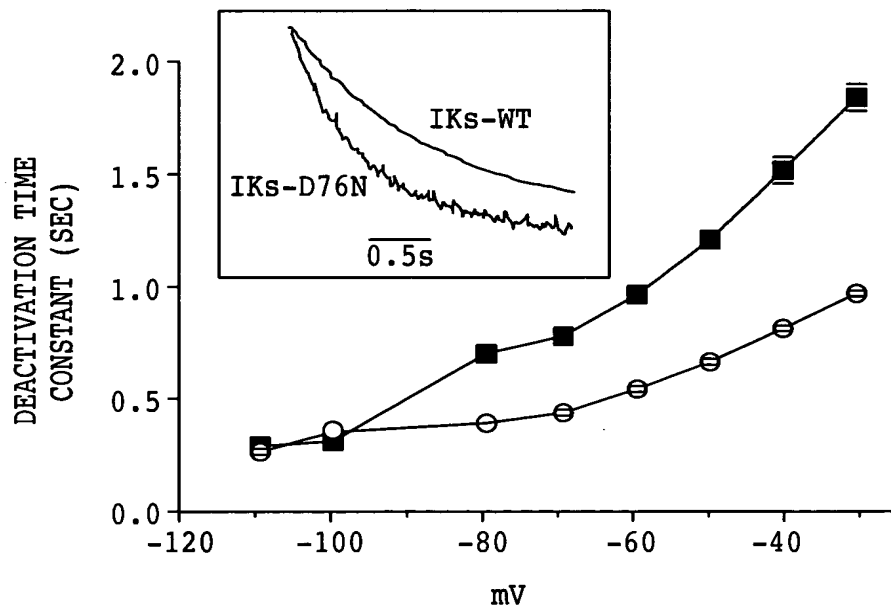


FIG. 15D

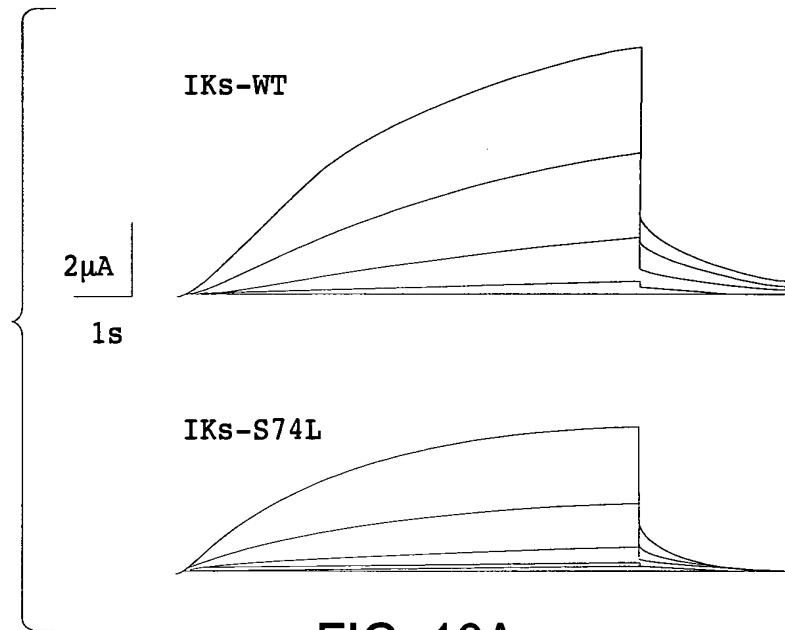


FIG. 16A

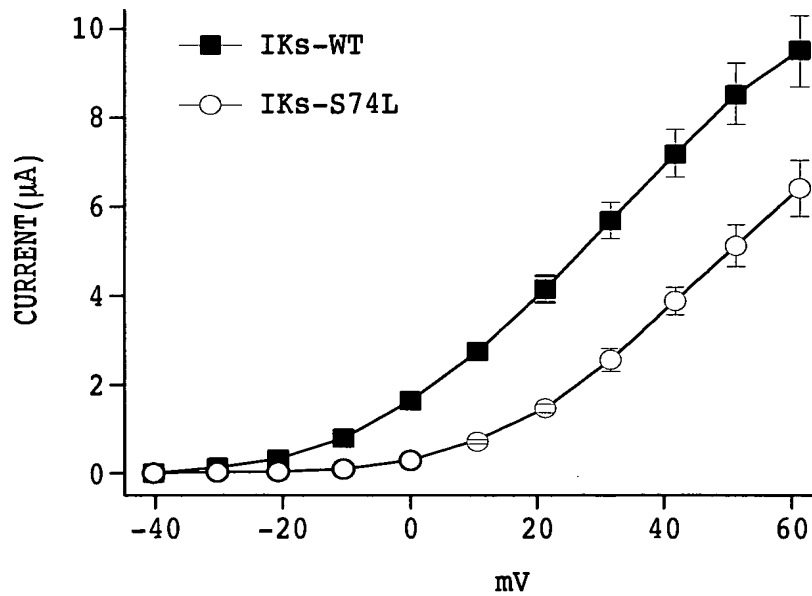


FIG. 16B

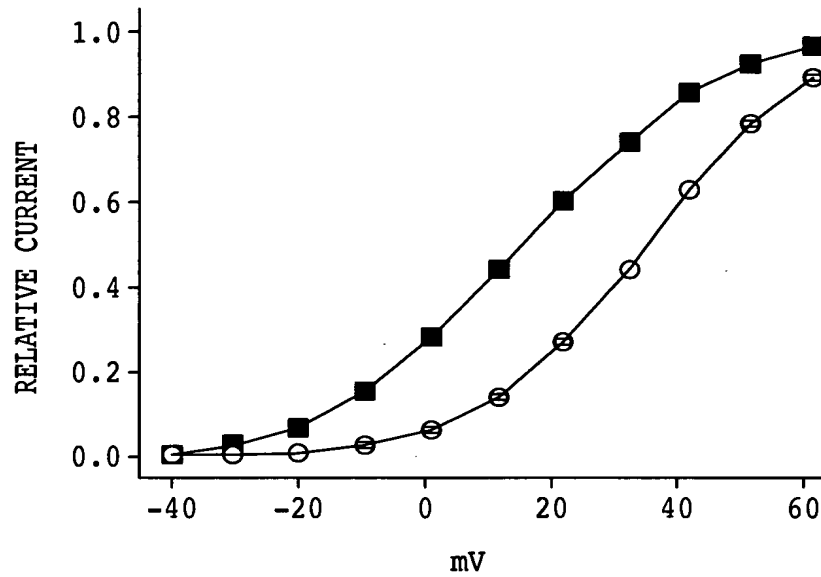


FIG. 16C

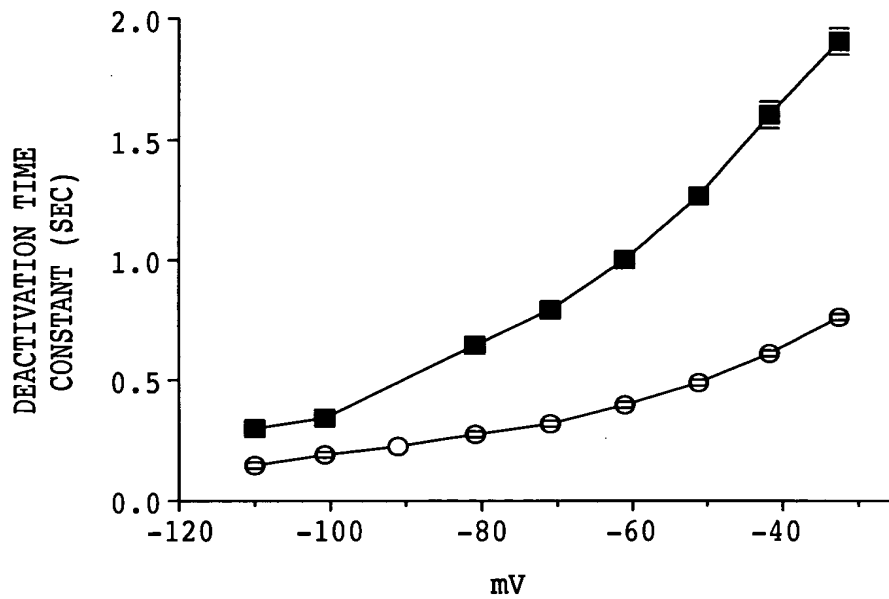


FIG. 16D

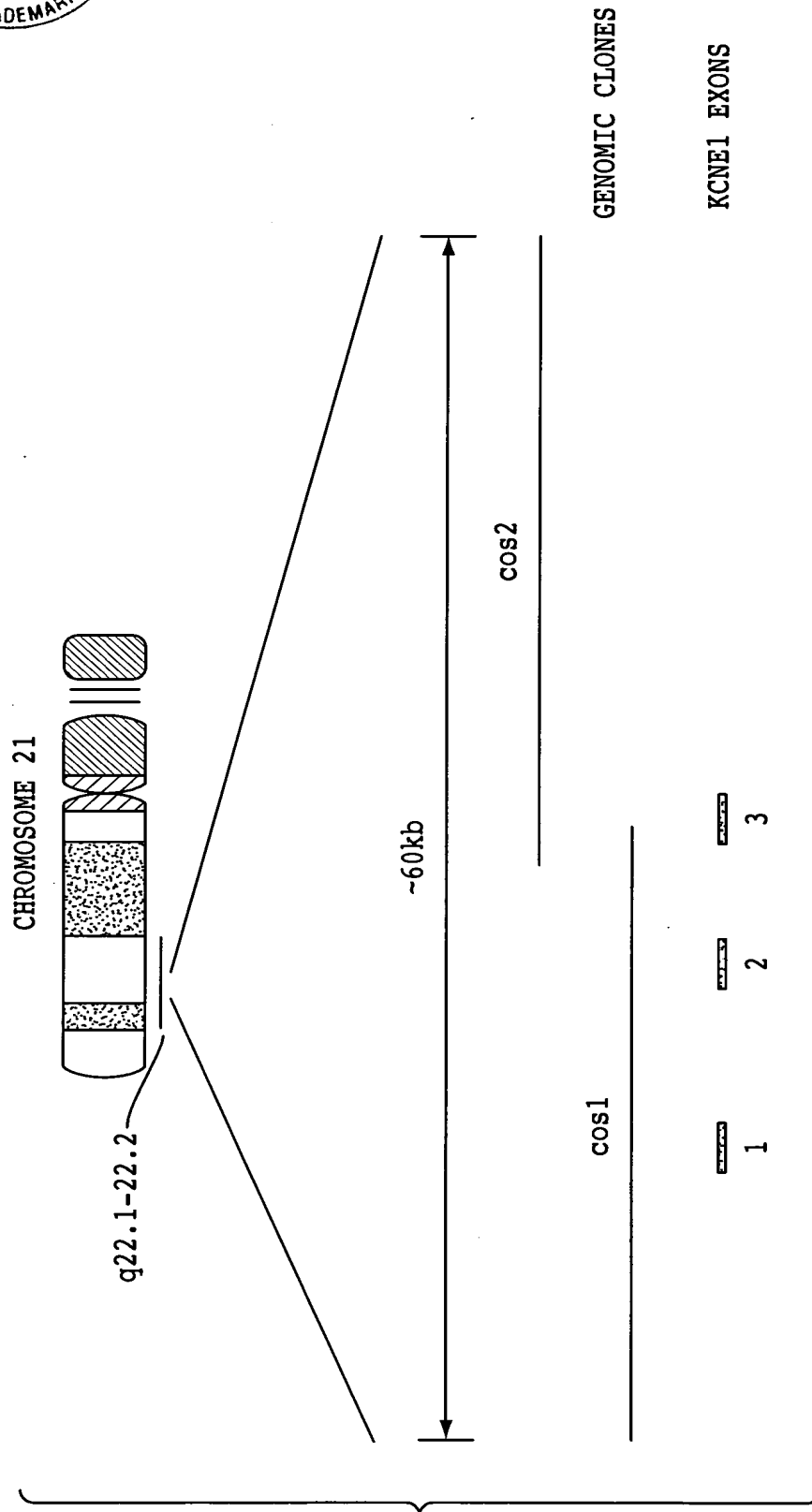


FIG. 17

25



ACACCCGGCTCTCTCGGCATCTCAGACCCGGGAAAAATCCCTCTGCTTTCTCTGGCCAGTTTCACACAATCATCAGGTGAG-81
CCGAGGATCCATTGGAGGAAGGCATTATCTGTATCCAGAGGAAATAGCCAAGGATATTCAGAGGTGTGCCTGGGAAGTTTG-162
AGCTGCAGCAGTGGAACCTTAATGCCCAGGATGATCCTGTCTAACACCACAGCGGTGACGCCCTTTCTGACCAAGCTGTGG-243
CAGGAGACAGTTCAGCAGGGTGGCAACATGTCTGGGCCTGGCCCCAGGTCCCCCGCAGCGGTGACGGCAAGCTGGAGGCC-324
Q E T V Q Q G G N M S G L A R R S P R S G D G K L E A -44
CTCTACGTCCTCATGGTACTGGGATTCTTCGGCTTCTTCACCTGGGCATCATGCTGAGCTACATCCGCTCCAAGAAGCTG-405
L Y V L M V L G F F G F F T L G I M L S Y I R S K K L -71
GAGCACTCGAACGACCCATTCAACGTCTACATCGAGTCCGATGCCTGGCAAGAGAAGGACAAGGCCTATGTCCAGGCCCGG-486
E H S N D P F N V Y I E S D A W Q E K D K A Y V Q A R -98
GTCTGGAGAGCTACAGGTCGTGCTATGTCTGTTGAAAACCATCTGGCCATAGAACAACCAACACACCTTCCTGAGACG-567
V L E S Y R S C Y V V E N H L A I E Q P N T H L P E T -125
AAGCCTTCCCCATGAACCCACCACTGGCTAACTGGACACCTCTGCTGGNNNNAGATTTTCTAATCACATTCTCTCA-648
K P S P *
TACTCTTTATTGTGATGGATAACCACTGGATTTCTTTTTGGCTGTTGTAANGGGTGAGGGGTGGATTAATGACACTGTTTCA-729
CTGTTTCTCTAAAATCACGTTCTTTTGTGATAGACTGTGAGTGTCCCCATATCTGTCCCTGCCTTGCTAAATTTAGCA-810
GAATCCCTGAGGACATGGCCTCTGAGAATAGCAGCTGCATTTCCAGACTCCCTTGCAAGGTGTGTGACTAAG-891
CCCTGGCCAGTAGGCATGGAAGTGAAGACTGTAATGTCCAAGTAATCCTTGGAAGAAAAGAACGTGCCCTTAACCTA-972
TGTCTGCTTCCAGTGGCTGGATGTGGAGGAGGTGGAGAGCAGTTATGAGACTGGGAAAGTTCGGGGCACTCAAAGAGCC-1053
ACACACATCTGGGCCTGGGCGACGTGGATCCTCCTTACCACCCACCAGGCCAGATTTACAGGAGAGAGAAATCCACTCCAC-1134
TCTTCTTAAGCCACTGTTATTCTGATCTCTGTTAAGGTGCGAGAATCAATGCCCTTACTGATACACCTACCTTATAGGAC-1215
TGAACCTAAAGGCATGACATTTCCATACTTGTACAAGCACACACTGATTCTGCCCTTGTCACTTCTGTGCTCACTCTTGT-1269
GGCTCTATCTCCTCCTGCCCTTCCGCCTTCCACTCCTCCCTTGACCCATCCTGCACACATCTCCCTGAAAACACACAGG-1377
CACATACTCATATACATAGACACACATACACCTCAATCTAGAAAGAACTTGCTTTGTACAGGGCTGAGATGGAGGAG-1458
AAAAAATGCCCCCTTCAAGTGCATACCAAGGGGAAGGTGCTCGGTCACTGTGGGAGCAGGGAAAGTGGCCCCACTCCC-1539
CGAGAGCCAGGGGAAGGAGTGGCTCTGGGCAGAGAGGGACACATAGCACTGGGGTGGCAGGTCCTTTTGAGGTGATGGGCC-1620
GGTTTGTGAGATGAATTGTATCCCCCAAAAGACAGGTACCTTCAATGTGACCTAATTGGGAAATAGAGTCTTTGCAGAT-1701
G(A)n -1702

FIG. 18